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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,913	06/23/2003	Patricia Gordon	GP087-04.CN1	8083

21365 7590 06/27/2006

GEN PROBE INCORPORATED
10210 GENETIC CENTER DRIVE
SAN DIEGO, CA 92121

EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,913	GORDON ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,8,11 and 13-15* is/are pending in the application.

4a) Of the above claim(s) *11 and 13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/26/04; 8/13/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on May 4, 2006 is acknowledged.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 2, 4, 5 and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

Claims 1, 2, 4, 5 and 8 all use 70% complementary language in order to encompass a genus of nucleic acids which are different from those disclosed in the

specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID Nos. Thus, applicant has express possession of only a few particular sequences in an immense genus. Just the genus of 70% alterations in the 28 nucleotides of SEQ ID NO: 5 would have 125,318,793,600 different permutations, with the complete genus of the undefined 72 nucleotides in the 100 nucleotide sequence adding 2.2×10^{43} more different possibilities. Here, no common element or attributes of the sequences are disclosed. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations of having 70% identity but retainining specificity for HPV 16 and not HPV 18 is provided.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the sequences using the 70% language lacks any specific structure. This is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the specific sequence of SEQ ID NO: 5 and the other listed sequences, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "70% complementary to 10 contiguous bases", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a hybridization probe with specificity for HPV 16, without any definition of the particular sequences necessary for this specificity.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which have specificity for HPV 16. Therefore, the claims fail to meet the

written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 2, 4, 5 and 8 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Brennan et al (U.S. Patent 5,474,796).

Brennan teaches the formation of an array which comprises every single 10-mer (see column 9, lines 53-55). This complete set of 10-mers necessarily and inherently comprises all of the 10-mers of claims 1, 2, 4, 5 and 8 and would inherently comprise all the 10 mers which are capable of hybridizing to the selected sequences with the required specificities.

6. Claims 1, 2, 5 and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by Gudibande et al (U.S. Patent 5,597,910).

Gudibande teaches a sequence, SEQ ID NO: 4, which will hybridize to HPV 16 (see column 20) but will not hybridize to HPV 18. SEQ ID NO: 4 has a region of 21

nucleotides of 100% identity with the claimed SEQ ID NO: 5 and is 30 nucleotides in length. The alignment between the sequences is shown below where the claimed SEQ ID NO: 5 is the query and the Gudibande SEQ ID NO: 4 is the Sbjct.

```
Score = 41.1 bits (21),  Expect = 0.045
 Identities = 21/21 (100%), Gaps = 0/21 (0%)
 Strand=Plus/Plus

Query  1   GAACAGCAATACAACAAACCG  21
           |||||||||||||||||||||
Sbjct  10  GAACAGCAATACAACAAACCG  30
```

With regard to claim 2, Gudibande teaches formation of a hybrid with a target region (see column 25, example 10, where the oligonucleotide is hybridized to target in a PCR reaction).

With regard to claim 5, Gudibande teaches a HPV 18 probe (see column 20) which has 22 nucleotides of identity with SEQ ID NO: 45. The alignment between the sequences is shown below where the claimed SEQ ID NO: 45 is the query and the Gudibande SEQ ID NO: 6 is the Sbjct.

```
Score = 43.0 bits (22),  Expect = 0.018
 Identities = 22/22 (100%), Gaps = 0/22 (0%)
 Strand=Plus/Plus

Query  1   GGAAAAACTAACTAACACTGGG  22
           ||||||||||||||||||||||
Sbjct  9   GGAAAAACTAACTAACACTGGG  30
```

With regard to claim 8, Gudibande further teaches an oligonucleotide which is 30 nucleotides in length and which has 23 nucleotides in common with SEQ ID NO: 121 (see column 20). The alignment between the sequences is shown below where the claimed SEQ ID NO: 121 is the query and the Gudibande SEQ ID NO: 5 is the Sbjct.

```
Score = 44.9 bits (23),  Expect = 0.005
 Identities = 23/23 (100%), Gaps = 0/23 (0%)
 Strand=Plus/Minus

Query  1   TTATTAATAAGGTGCCTGCGGTG  23
           |||||||||||||||||||||||
Sbjct  23  TTATTAATAAGGTGCCTGCGGTG  1
```

7. Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Bouma et al (U.S. Patent 5,484,699).

Bouma teaches a sequence, SEQ ID NO: 95, which will hybridize to HPV 16 (see column 22, example 19) but will not hybridize to HPV 18. SEQ ID NO: 95 has a region of 20 nucleotides of 100% identity with the claimed SEQ ID NO: 5 and is 24 nucleotides in length. The alignment between the sequences is shown below where the claimed SEQ ID NO: 5 is the query and the Bouma SEQ ID NO: 95 is the Sbjct.

```
Score = 39.1 bits (20),  Expect = 0.17
 Identities = 20/20 (100%), Gaps = 0/20 (0%)
 Strand=Plus/Plus

Query  9   ATACAACAAACCGTTGTGTG  28
           ||||||||||||||||||||
Sbjct  1   ATACAACAAACCGTTGTGTG  20
```

With regard to claim 2, Bouma teaches formation of a hybrid with a target region (see column 22, example 19, where the oligonucleotide is hybridized to target in an amplification reaction).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 2, 4, 5 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al (WO 94/26934) in view of Hogan et al (U.S. Patent 5,030,557) and further in view of Dopazo et al (J. Virol. Meth. (1993) 41:157-166).

Brown teaches a composition for amplifying an HPV Type 16 target nucleic acid comprising an amplification oligonucleotide and a polymerase where the amplification oligonucleotide also comprises a 5' promoter sequence. Specifically, SEQ ID NO: 27 (HPV 120) meets the oligonucleotide test (page 11, lines 25-27) and the composition is taught on pages 12-13, where the oligonucleotide is combined with reagents including

AMV-RT and T7 RNA polymerase, both of which are nucleic acid polymerases. Brown expressly teaches formation of kits (page 4, lines 23-24).

Brown does not teach the specific probes of SEQ ID NOs: 1, 5, 45, 85 and 121 but does teach sequences comprising these probe sequecnes. Brown does not teach the use of helper probes.

Brown teaches a sequence comprising SEQ ID NO: 1 beginning on page 25, line 29, nucleotide 26. Brown teaches a sequence comprising SEQ ID NO: 5 beginning on page 25, line 36, nucleotide 16. Brown teaches a sequence comprising SEQ ID NO: 45 beginning on page 27, line 48, last nucleotide in line. Brown teaches a sequence comprising SEQ ID NO: 85 beginning on page 25, line 43, nucleotide 339 in the reverse orientation. Brown teaches a sequence comprising SEQ ID NO: 121 beginning on page 27, line 53, nucleotide 31.

Hogan teaches methods for enhancing hybridization including the use of helper probes (column 4, lines 44-68). Hogan also teaches requirements for helper probes (columns 5 and 6).

Dopazo evidences that the ordinary practitioner, in 1993, had access to Dopazo's computer program (which was one of many free and commerically available primer selection programs) ("We describe a computer program, availabe upon request (see page 158)." Further, Dopazo evidences the ability of the computer to select any primers which are common to a group of sequences but to exclude primers which are non-specific as desired (see page 159, last paragraph to page 160, first paragraph). Dopazo specifically suggests selection of primers in HPV (see page 157). An ordinary

practitioner, motivated by Brown to select primers to detect HPV 16 or 18, would have been able to utilize the available computer program of Dopazo to select primers that were species specific, of which SEQ ID Nos: 1, 5, 45, 85 and 121 are simply structural equivalents in that set of primers and therefore prima facie obvious under Deuel.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to utilize the type specific selection procedure of Brown for selection of additional sequences from the disclosed sequence of Brown. Brown expressly notes that "Primer selection for high level amplification is basically a directed trial and error process. To define a first set of primers a span of 400 bases (with beginning and ending sites outside the spliced region) was selected by designating the first 10-30 nucleotides at the 5' end of the E6 gene beginning with the ATG codon and counting off 400 bases, then selected as primers the next 10-30 bases. Note that for each pair, at least one of the primers must contain a promoter for transcription. (page 12, lines 8-14)". Brown further notes that "The primer pairs are tested for their amplification efficiency. To optimize, the second primer position is held stationary and the first primer is moved arbitrarily 20 bases toward the second (thereby decreasing the interprimer span, e.g. the bases between the position of the 3' end of the first primer and the 5' end of the second primer, by 20 bases to 380 bases). Fine tuning is accomplished by walking the primers from the best pairings by 2-5 base jumps (page 12, lines 18-24)". An ordinary practitioner would have been motivated to optimize the primers of Brown as taught by Brown for the benefits of type specific selection of HPV

as taught by Brown (abstract)". An ordinary practitioner would have found all of the claimed primers functionally and structurally identical.

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the Brown hybridization method for detection of HPV with the helper probe methods of Hogan since Hogan teaches that "Thus, by using a properly selected helper oligonucleotide, the rate of hybridization between the probe and its complementary sequence in the targeted nucleic acid can be substantially increased and even permit hybridization to occur at a rate and under conditions otherwise adequate for an assay where, without the use of the helper, no substantial hybridization can occur.(column 4, lines 36-43)." Hogan explicitly states that the helper probe need not be targeted at a unique sequence (column 7, lines 40-42). An ordinary practitioner would have been motivated to add the use of a helper probe in order to increase the rate of hybridization.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers and probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of HPV, and in particular for diagnosis of the presence of the hepatitis virus strains 16 and 18, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Conclusion

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Tyan et al (J. Clin. Microbiol. (1993) 31(1) :53-56) teaches a sequence which encompasses SEQ ID Nos : 1 and 85 (see page 55, column 2, figure 3).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637
6/13/06